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CLINICOPATHOLOGICAL PROFILE OF MALE BREAST CANCER: 3 YEAR STUDY.

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Abstract:

Background: Breast cancer in men is a rare disease and is not commonly seen in day today oncology practice. It accounts for less than 1% of all cancers in men and less than 1% of all diagnosed breast cancer. Approximately 10% of men with breast cancer have a genetic predisposition and BRCA 2 is the most associated gene mutation. Due to relative rarity of male breast cancers, prospective randomized trials are lacking and most information on breast cancer in men has been collected from retrospective studies spanning several decades and treatment recommendations have been extrapolated from results of trials in female patients.

Materials and Methods: The purpose of this retrospective study was to analyze various clinicopathological features of male breast cancer presenting to our department between January 2016 to ending December 2018.

Results: Data from 5 male breast cancer cases was analyzed. Male breast cancer accounted for 2.64% of all breast cancer cases. The mean age at diagnosis was 60.2 years. Left breast was involved in 80% cases. Invasive duct carcinoma was the predominant histopathological variant in all cases.60% cases had modified SBR Grade ll tumors whereas lymphovascular invasion was seen in 60% cases. 60% cases presented with stage ll disease, whereas20% cases each had stage lll and IV breast cancer respectively. All (100%) cases were hormone receptor positive(ER+, PR+) and Her nu 2 overexpression was seen in 20% cases.

Conclusion: Male breast cancer though a rare disease does exist. Social programs aimed at providing education and awareness about male breast cancer will lead to earlier presentation of patients to heath care professionals and hence early diagnosis.

Keywords: Male breast cancer, Clinicopathological features, Estrogen receptors, Progesterone receptors,Her nu 2 expression,Invasive ductal carcinoma.

Introduction

Breast cancer in men is a rare disease and is not commonly seen in day today oncology practice. Male breast cancer accounts for less than 1% of all cancers in men and less than 1% of all diagnosed breast cancers [1]. The incidence of male breast cancer is variable in different regions. In Northwest Europe and North America it is approximately 1/100,000 as compared to <0.5/100,000 in Japan [2]. In Central and Eastern Africa breast cancer rates are higher and reach 6% of cancers in men, which could be expected by hyperestrogenism due to endemic hepatic infectious disease [3] .The etiology of male breast cancer is also not clear, but hormonal levels may play a role in the development of this disease. Testicular abnormalities like undescended testis, congenital inguinal hernia, orchitis and infertility have been consistently associated with elevations in breast cancer risk. Klinefelter's syndrome in which patients carry XXY chromosomes may be present in 3%-7% of men with breast cancer giving males with Klinefelters syndrome 50 fold greater risk over the general male population. Men with a family history of breast cancer in a female relative have a 2.5 times odds of developing breast cancer. Approximately 15-20% of men with breast cancer report a family history of breast or ovarian cancer [2]. Approximately 10% of men with breast cancer have a genetic predisposition and BRCA 2 is the most associated gene mutation. Among male BRCA2 mutation carriers the estimated lifetime risk of breast cancer is 5-10% compared with

a general population risk of 0.1%.The life time risk of male breast cancer with BRCA1 mutation is approximately 1-5% [2]. Data from literature suggest that male breast cancer has biological differences compared with female breast cancer. Morphologically, it is similar to female breast cancer because it is represented mostly by infiltrating ductal carcinoma, although with lower incidence of invasive lobular carcinomas. Moreover male breast cancers are usually diagnosed at a more advanced age and stage than female breast cancers, with larger tumor size and lymph node involvement. Evidence suggests hormone receptor positivity for both ER and PR being proportionally higher in male breast cancer (75-90%) than in female breast cancer. Updated studies using standardized HER 2 assessment methods indicate HER 2 expression in male breast cancer up to 15% versus 25-30% in female breast cancer [4] .Due to relative rarity of male breast cancers, prospective randomized trials are lacking and most information on breast cancer in men has been collected from retrospective studies spanning several decades and treatment recommendations have been extrapolated from results of trials in female patients [2],[3] .

MATERIAL AND METHODS

The present retrospective study was carried out in the Department of Radiation oncology, Government Medical College Srinagar, Kashmir, India. All male patients who reported to our department from January 2016 to ending December 2018 were screened and cases with histopathological diagnosis of male breast cancer were included in this study. The data collected focused on:

- **Socio demographic data**: Age at diagnosis, marital status, any family history of breast cancer or any other malignancy.
- **Clinical data**: All necessary relevant details like pre surgical investigations, details of metastatic workup, nature of surgery done with intraoperative findings, any neo adjuvant chemotherapy received, Stage of disease at diagnosis ,Complete histopathological details like type of malignancy, Modified Scarff Bloom Richardson Grade of tumor, Lymph node metastasis, Lymph vascular invasion, Status of hormone receptors (ER, PR), HER nu 2 receptor overexpression , adjuvant treatment etc.

American joint committee on cancer TNM staging system for breast cancer was followed to determine the stage of the disease. The data was analyzed for various sociodemographic and clinicopathological entities.

RESULTS

After proper scrutiny, data from 5 male breast cancer cases was included in the present study. Male breast cancer accounted for 2.64% of all breast cancer cases reported to our department during the study period. The youngest patient was 43 years old and the oldest was 66 years of age. 4 (80%) cases were more than 60 years of age and the mean age at the time of diagnosis was 60.2 years. All male cancer patients were married .Left breast was more commonly involved in 4(80%) patients whereas 1(20%) patient had breast cancer diagnosed in right breast.

The most common symptom was palpable breast lump in all 5(100%) patients, with associated pain in 1(20%) and nipple retraction in 1(20%) cases. The most common location of tumor was beneath nipple sub areolar region 3(60%). None of the male breast cancer patient in our study had any family history of breast cancer. Invasive duct carcinoma (IDC) was the predominant histopathological variant in all 5(100%) patients. Majority 3(60%) patients had modified Scarff Bloom Richardson Grade ll score whereas 2 (40%) had grade l score, [Table 1].Lympho vascular invasion was seen in 3(60%) of our cases on histopathology.

In our study majority 3(60%) cases had tumor size between >2 cms but ≤ 5 cms and 2(40%) cases had tumor size >5 cms. After definitive surgery 3(60%) patients had metastasis in 1 to 3 lymph nodes, whereas 1(20%) patient had metastasis in ≥ 10 lymph nodes and the percentage of positive lymph nodes in our study was 27.27%. Most of the patients 3(60%) presented with stage ll disease, whereas 1(20%) patient each had stage lll and stage lV breast cancer respectively.

All 5(100%) cases in our study had tumors with positive hormone (ER, PR) receptors status, whereas Her nu 2 over expression was positive in 1(20%) case only. Hence 4(80%) cases in our study were ER+PR+ Her nu 2 –ve and 1(20%) case was ER+PR+ Her nu 2 +. Three (60%) patients in our study had underwent upfront surgery whereas 1(20%) patient underwent Modified radical mastectomy after neoadjuvant chemotherapy. In 1(20%) patient surgery was not done in view of metastatic disease and tru cut biopsy from breast was done to establish diagnosis and for molecular studies.

Table 1: Clinicopathological characteristics of male patients with carcinoma Breast.

Characteristics		n	%
Age in years	≤ 60	1	(20%)
	>60	4	(80%)
Marital status	Married	5	(100%)
	Un Married	0	(0%)
Presentation	Breast Lump	5	(100%)
	Pain	1	(20%)
	Nipple Retraction	1	(20%)
Tumor Site	Right Breast	1	(20%)
	Left Breast	4	(80%)
Family History	Present	0	(0%)
	Absent	5	(100%)
Post Surgical Histopathology	Infiltrating Ductal Carcinoma	5	(100%)
	Others	0	(0%)
Tumor Grade	|	2	(40%)
	||	3	(60%)
	|||	0	(0%)
Lympho vascular infiltration	Present	3	(60%)
	Absent	2	(40%)
Hormone Receptors	ER+	5	(100%)
	PR+	5	(100%)
	ER+ PR+	5	(100%)
HER-2 neu Status	Positive	1	(20%)
	Negative	4	(80%)
Clinical Stage	|	0	(0%)
	||	3	(60%)
	|||	1	(20%)
	IV	1	(20%)
Post Surgical Positive Lymph Node Status	0	0	(0%)
	1 - 3	3	(60%)
	4 - 9	0	(0%)
	≥ 10	1	(20%)
	Un operated	1	(20%)
Tumor Size (cm)	≤ 2	0	(0%)
	>2 - ≤ 5	3	(60%)
	>5	2	(40%)

DISCUSSION

Male breast cancer accounted for 2.64% of all breast cancer cases reported to our department during the study period which is slightly higher than normally reported in the literature. Pothamsetty R K et al [1] also reported 2.5% of all breast cancer cases as male breast cancer whereas Hariharan N [5] and Sundriyal D et al [6] reported 0.7% and 1.03% of all breast cancer cases as male breast cancer cases in their respective studies. In our study mean age at diagnosis was 60.2 years. Khalil A I et al [7] reported mean age among six male breast cancer patients as 63.3 years whereas Staruch R M T et al [8] reported a higher mean age of 69 years at diagnosis. Positive family history of breast cancer has been associated with increased risk of developing male breast cancer however none of our patients had any family history of breast cancer. Similar findings were reported by Sundriyal D et al [6] who in a retrospective study of 10 years period identified 18 male breast cancer patients but did not find any case of male breast cancer with a positive family history of breast cancer, whereas Masci G et al [4] reported 18.7% male breast cancer patients having family history of breast cancer.

All 5(100%) patients in our study had invasive ductal carcinoma (IDC) as their histopathological feature. Similar findings were reported by Pothamsetty RK et al [1] Hariharan N [5],Sundriyal D et al [6] and Staruch R M T et al [8] where also invasive ductal carcinoma was seen in 100% male breast cancer patients under analysis.

Majority 3(60%) of patients in our study had modified Scarf Bloom Richardson Grade ll tumors. Khalil A I et al [7] in his study also reported majority cases 66.7% with SBR Grade ll tumors. In our study 3(60%) patients presented with stage ll disease. Similar finding was reported by Ram D et al [9] who in a study on 27 male breast cancer patients reported stage ll as most common stage (66.7%) at presentation. All 5(100%) patients in our study were hormone receptor(ER, PR) positive. Similar findings were reported by Staruch R M T et al [8] ,who reported 100% patients with positive ER status. Masci G et al [4] reported ER positivity in 96.7% cases and PR positivity in 92.3% cases, whereas Hariharan N [5] found hormone receptor status(ER and/or PR) positive in 97% cases. Ram D et al [9] also reported 77.8% male breast cancer cases with positive hormone receptor status.

Like any other study our study has its limitations like: single center experience, small sample size, retrospective study of 3 years only. A comprehensive multi institutional study over a long period is required to exactly delineate the behavior of the disease and to better understand the demographic, clinical, pathological, and molecular spectrum.

CONCLUSION

Male breast cancer though a rare disease, does exist. Breast cancer affects an individual financially, psychologically and socially. Social programs aimed at providing education and awareness about male breast cancer in a population will lead to earlier presentation of patients to health care professionals and hence early diagnosis of the disease.

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